

Patent

U.S. Ser. No. 10/054,638

Response to the Office Action mailed 12 December 2007

Appendix 6



ELSEVIER

Vaccine 20 (2002) 526-531

www.elsevier.com/locate/vaccine

Modeling the economic benefits of an AIDS vaccine

David Bishai^{a,*}, Maria K. Lin^b, C.W.B. Kiyonga^c

^a Department of Population and Family Health Sciences, Johns Hopkins University Bloomberg School of Hygiene and Public Health, 615 N. Wolfe St., Baltimore, MD 21205, USA

^b Department of International Health, Johns Hopkins University Bloomberg School of Hygiene and Public Health, 615 N. Wolfe St., Box 231, Baltimore, MD 21205, USA

^c Office of the Minister of Health, Kampala, Uganda

Received 19 October 2000; received in revised form 16 July 2001; accepted 16 July 2001

Abstract

Economic models were used to describe the potential for an AIDS vaccine to prevent medical spending and lost productivity throughout the world. In terms of avoided medical spending, preventing 75% of the AIDS risk for 10 years in one adult male is estimated to be worth US\$ 343 in western Europe, US\$ 4.59 in south and SE Asia, and US\$ 2.67 in sub-Saharan Africa. The expected medical savings from a 75% effective vaccine would exceed US\$ 25.00 per person for over 700 million people. Although an AIDS vaccine would save more lives in poverty stricken areas, it would save more money in developed countries. The mismatch between the public health needs and market forces is highlighted by this model. © 2001 Published by Elsevier Science Ltd.

Keywords: AIDS; HIV; Vaccine; Economics; Demand; Epidemiology; Costs

1. Introduction

This paper attempts to answer the question, "What would be the expected medical savings and labor productivity savings if an AIDS vaccine were administered to the various regional populations of the world?" The answer to this question will help individuals in both the private and public sectors to prepare for the efficient and equitable development and distribution of an AIDS vaccine to slow the epidemic. Creating more effective policies requires advance preparation built on an understanding of the future market for AIDS vaccines.

This paper projects the results of simple cost-benefit criteria as applied to the latest data on the epidemiology and economics of this disease. It would be unusual and undesirable if cost-benefit considerations exactly determined whom in the world eventually received AIDS vaccine. Nevertheless, limited budgets make economic considerations an unavoidable part of setting priorities in disease control. The exercises presented here attempt to model future cost-benefit studies of AIDS vaccines by applying cost-benefit analysis to a hypothetical AIDS vaccine of 75% effectiveness with a

10-year duration. We recognize that unforeseen changes in the fundamental determinants of demand for an AIDS vaccine will occur between now and the time when a vaccine is released, but the current model permits a timely preview of many economic issues surrounding HIV vaccine. Although there is no vaccine available yet, there is already high interest in establishing today a policy framework to speed access to an AIDS vaccine once one is discovered [1-3]. This model is intended to inform policy-makers about what future cost-benefit analyses of AIDS vaccine may show.

2. Methods

2.1. Health sector versus societal perspective

Economic benefits of AIDS vaccine are modeled as prevented expenditures related to disability and death from AIDS. Two alternative models depict the standard perspectives on the costs of an illness: (1) the *health sector perspective* in which the cost of an illness equals the net present value of the sum of all medical care costs incurred; and (2) the *societal perspective* in which the lost economic productivity is included as well as medical costs [4]. The

* Corresponding author. Tel.: +1-410-955-7807; fax: +1-410-955-0792.
E-mail address: dbishai@jhsph.edu (D. Bishai).

full societal impact of AIDS also includes intangible costs of AIDS in terms of suffering and social upheaval that are potentially quite large but difficult to measure. A country's decision to purchase the AIDS vaccine could be motivated by either of these two perspectives on the cost of disease. The strategy that currently appears to be most prevalent for vaccine purchase decisions by health ministries is the health sector perspective in which the government health ministry is allocated a fixed budget and asked to allocate purchases for all items (often including vaccines) to maximize a population's health under that budget.

2.2. AIDS vaccine characteristics

Assumptions about the characteristics of AIDS vaccine are based on known properties of current vaccines for other diseases. AIDS vaccines under consideration could have three potential effects on the disease: (1) reduce pre-exposure susceptibility to infection; (2) slow disease progression to AIDS; and (3) reduce virus shedding. Our model will consider only the first effect because it is both simplest to model and because personal susceptibility is the foremost concern in a purchase decision by an uninfected person and/or a clinician deciding on their behalf.

In the baseline model, efficacy is assumed such that 75% of recipients who receive a complete course develop 100% protective immunity whether immunized pre- or post-exposure. Vaccine developers and their funders have no expectation that the initial vaccine trials will achieve sterilizing immunity in all recipients. There is widespread concern that a vaccine that protects only half of its recipients may not be licensed for fear that it could lead to offsetting risk behavior. A baseline efficacy of 75% was chosen to represent a vaccine that was of intermediate protection.

It is assumed that the vaccine's protection will last at least 10 years. If the initial generation of AIDS vaccine turns out to have lower efficacy and duration, the model could be adapted accordingly. The models do not take into account the possibility that a vaccine may lower the degree of shedding of infectious particles or offer therapeutic benefit.

Our model profiles potential vaccine consumers by first dividing the world's population into major geographical regions. Within each region, the general population is disaggregated by gender and by age group (0–14, 15–64, >65).

2.3. Modeling vaccine benefits

The following model of benefits predicts that financial benefits from AIDS vaccines depend on local economic factors:

benefit of V_j to the health sector

$$= PV[E \times I_{jt} \times (1 + N_{jt}) \times HC_{jt}] \quad (1)$$

where PV denotes present value computed at a 3% discount rate for a 10-year duration; V_j a decision to vaccinate everybody in group "j" where j is defined by age, gender, and world region; E vaccine efficacy from 0 to 100%, assumed = 75% for exactly 10 years in baseline analysis; I_{jt} incidence of AIDS or likelihood that average person in group j will develop AIDS in year t ; N_{jt} the number of active secondary cases caused by group j and detected in year t ; HC_{jt} health care costs in year t for group j . All health care costs are attributed to the same year in which a case develops.

Eq. (1) corresponds to the "health sector perspective"—it reflects a health minister's efforts to minimize the government's financial burden from HIV.

Economic benefits are computed from a societal perspective that includes lost productivity as follows:

$$\begin{aligned} \text{benefit of } V_j \text{ to society} &= PV[E \times I_{jt} \times (1 + N_{jt}) \\ &\quad \times (HC_{jt} + W_{jt})] \end{aligned} \quad (2)$$

where W_{jt} are lost wages in year t for group j due to death and disability from AIDS.

Eq. (2) corresponds to the "societal perspective"—it reflects the considerations of a minister of finance searching for investments to both curtail medical costs and improve economic productivity.

To indicate the degree of inequity in vaccine distribution inherent in these two simple algorithms, both models were recalculated to estimate benefits throughout the world based on each group's AIDS incidence, but with monetary values for medical spending and lost productivity from western Europe. This corresponds to an "equity perspective" in that regional variation in the benefit from AIDS vaccine reflects only variation in incidence and rates of disease transmission—not the vagaries of local medical spending and GDP.

Collapsing the complex dynamics of an AIDS epidemic into a single equation offers tremendous simplicity and enables transparent comparisons of vaccine benefits across geographic regions.

The models were run using secondary data for each regional subgroup on HIV incidence [5,6], medical care costs [7], and GDP/capita [8]. People whose estimated benefits exceeded a given price were considered to be potential buyers at that price. Cumulative numbers of buyers were tallied whose modeled benefits exceeded a range of possible AIDS vaccine prices from US\$ 1.00 to 100.00. Population estimates used the latest demographic data for cohorts defined by age and sex [9]. The equations underlying the model required data on health care costs, productivity costs, and vaccine administration costs for each subgroup. Table 1 summarizes estimates of costs incurred per AIDS case used in the baseline models. Table 1 shows both the present discounted value of a single HIV seroconversion in terms of medical spending, and present discounted value of lost productivity. Details on how each of these estimates was assembled is presented in a separate publication [10].

Table 1
Lifetime value lost per new case of AIDS by age and region^a

Region	Infants/toddlers (age 0-4) (US\$)	School children (age 5-14) (US\$)	Average for adults (age 15-49) (US\$)
Western Europe, medical (societal ^b)	255014 (573552)	255014 (683102)	255014 (583263)
North Africa and middle east, medical (societal)	1335 (103300)	1335 (138368)	1335 (117525)
Sub-Saharan Africa, medical (societal)	38 (16140)	38 (21678)	38 (18386)
South and SE Asia, medical (societal)	441 (53829)	441 (72190)	441 (61277)
Eastern Europe and central Asia, medical (societal)	5035 (31274)	5035 (40298)	5035 (34934)
China, medical (societal)	1896 (10972)	1896 (14093)	1896 (12238)
Japan, medical (societal)	150591 (801166)	150591 (1024909)	150591 (821001)
South Korea, medical (societal)	67031 (218860)	67031 (271077)	67031 (223489)
East Asia and Pacific, medical (societal)	2820 (25151)	2820 (32831)	2820 (28266)
Australia and New Zealand, medical (societal)	122163 (409977)	122163 (508961)	122163 (418752)
North America, medical (societal)	299894 (650616)	299894 (771235)	299894 (661309)
Caribbean, medical (societal)	3322 (68946)	3322 (91515)	3322 (78101)
Latin America, medical (societal)	1942 (42683)	1942 (56694)	1942 (48366)

^a Numbers in cell are the lifetime value of medical savings from preventing a single case of HIV seroconversion. Numbers in parentheses add to the medical costs the lifetime value of productivity savings. All estimates are given in year 2000 US dollars and discounted at 3%. Parameters underlying these estimates are discussed elsewhere [10].

^b Societal refers to the sum of medical and productivity losses.

3. Results

Given the estimates of AIDS risk, vaccine efficacy, and the economic loss, the benefit from 10 years of 75% risk elimination is computed for each target group using Eq. (1) for the health sector perspective, and Eq. (2) for the societal perspective; see Tables 2 and 3. For example, sub-Saharan Africa results (Table 2) indicate that in terms of prevented medical spending, eliminating 75% of the AIDS risk for 10 years for an African man would be worth US\$ 2.67. In addition, benefits from both prevented medical spending and lost productivity (Table 3) show that eliminating 75% of the AIDS risk for 10 years for an African man would be worth US\$ 1531. Model results embodying market related

values of worth confirm the common perception that financial markets would value AIDS prevention more highly in established market economies.

The parenthesized values in Tables 2 and 3 were derived by substituting western European costs for the costs from the various regions to reflect the premise that all lives should be valued equally. This counts all AIDS consequences throughout the world on the same dollar value scale. These parenthesized values show that Africa, Asia, and the Caribbean are regions with the greatest opportunity to prevent AIDS consequences. This demonstrates the disparity between public health priorities and financial rewards: areas with the greatest opportunity to save lives are areas where there is the least financial reward to do so.

Table 2
Health sector perspective estimates^a

	Infants/toddlers (age 0-4) (US\$)	Children/teens (age 5-14) (US\$)	Women (age 15-49) (US\$)	Men (age 15-49) (US\$)
More developed countries				
Western Europe	31.61 (31.61)	105.39 (105.39)	87.13 (87.13)	342.87 (342.87)
Australia and New Zealand	-2.10 (0.19)	16.02 (38.02)	0.51 (5.64)	72.00 (154.87)
North America	87.94 (74.15)	262.94 (222.96)	209.51 (177.52)	850.66 (722.73)
Japan	-1.10 (0.69)	17.62 (32.41)	0.83 (3.97)	77.66 (133.07)
South Korea	-3.88 (-3.77)	16.12 (173.40)	1.19 (15.54)	31.05 (129.13)
Less developed countries				
North Africa and middle east	-0.41 (17.04)	-0.06 (82.63)	-0.15 (66.01)	0.89 (265.53)
Sub-Saharan Africa	-0.10 (2656.19)	1.07 (10513.90)	2.61 (20818.01)	2.67 (21238.58)
South and SE Asia	-0.30 (112.70)	1.23 (999.10)	1.32 (1051.71)	4.59 (2945.69)
East Europe and central Asia	-0.22 (13.66)	9.74 (518.01)	8.14 (437.36)	31.80 (1635.70)
East Asia and Pacific (excluding China, Japan, South Korea)	-0.34 (13.66)	1.40 (170.90)	0.46 (86.02)	6.12 (598.58)
China	-0.47 (4.19)	0.90 (188.12)	0.17 (90.04)	4.44 (663.44)
Caribbean	5.12 (430.80)	27.91 (2180.90)	36.63 (2849.86)	76.03 (5874.73)
Latin America	0.05 (71.09)	4.05 (597.18)	2.86 (440.87)	14.35 (1948.86)

^a Net expected benefit of vaccination by group and by region. Numbers in parentheses are the values that would be obtained if the ability to pay in that region were equal to that of western Europe. Negative values indicate that the savings to the medical sector from vaccination do not exceed vaccine delivery costs.

Table 3
Societal perspective estimates^a

	Infants/toddlers (age 0–4) (US\$)	Children/teens (age 5–14) (US\$)	Women (age 15–49) (US\$)	Men (age 15–49) (US\$)
More developed countries				
Western Europe	76.34 (76.34)	289.38 (289.38)	204.69 (204.69)	789.62 (789.62)
Australia and New Zealand	2.87 (5.69)	80.08 (108.92)	11.97 (18.33)	257.01 (359.63)
North America	195.71 (172.03)	682.81 (604.30)	467.07 (411.45)	1880.91 (1658.43)
Japan	11.41 (6.82)	143.16 (93.87)	22.35 (14.51)	441.18 (311.06)
South Korea	–3.62 (–3.21)	0.00 (473.22)	13.31 (40.97)	112.85 (300.76)
Less developed countries				
North Africa and middle east	6.61 (38.95)	44.61 (222.19)	30.15 (151.61)	122.10 (607.96)
Sub-Saharan Africa	167.64 (5974.66)	893.29 (28164.31)	1500.50 (47615.30)	1530.82 (48577.24)
South and SE Asia	23.40 (254.11)	282.47 (2677.11)	252.33 (2406.10)	707.43 (6737.97)
East Europe and central Asia	1.24 (31.34)	81.44 (1388.44)	59.48 (1000.96)	223.64 (3741.80)
East Asia and Pacific (excluding China, Japan, South Korea)	0.90 (31.34)	21.57 (458.63)	9.09 (197.38)	65.90 (1369.71)
China	–0.30 (10.04)	9.92 (504.75)	3.84 (206.57)	31.36 (1518.05)
Caribbean	116.11 (969.54)	782.33 (3842.79)	872.46 (6518.80)	1798.86 (13437.25)
Latin America	11.48 (160.52)	132.38 (1600.51)	83.21 (1008.99)	369.22 (4458.06)

^a Net expected benefit of vaccination by group and by region. Numbers in parentheses are the values that would be obtained if the financial consequences of HIV/AIDS in that region were equal to that of western Europe. Negative values indicate that the savings to the GDP from vaccination do not exceed vaccine delivery costs.

3.1. Cumulative numbers of vaccine users at different prices

Figs. 1 and 2 tally the cumulative number of people whose benefits exceed a range of possible prices for AIDS vaccine. Fig. 1 does this according to the health sector decision rule. Fig. 2 shows the curve that would be generated from the societal perspective.

For example, in Fig. 1, from a health sector perspective, one sees that close to 1 billion people today would reckon the benefits of a 75% effective, 10-year duration AIDS vaccine to exceed US\$ 10.00 based on the expected value of AIDS medical spending. At any vaccine price, a greater number of people reckon AIDS vaccine cost beneficial under the societal perspective as shown in Fig. 2.

3.2. Sensitivity tests

To test the robustness of the model to the estimates of vaccine effectiveness, the curves in Figs. 1 and 2 were re-estimated with the assumption that vaccine effectiveness was as high as 90% and as low as 50% retaining all other assumptions unchanged. The model did not incorporate the conjecture that vaccines with low rates of effectiveness could lead individuals to increase their risk behavior. These alternative curves are displayed as dotted lines in the figures. The sensitivity tests indicate that the less effective vaccine would attract similar numbers of potential buyers at prices that are generally half the size of a 75% effective vaccine. The model's sensitivity to vaccine effectiveness becomes more pronounced at higher prices. Other tests of sensitivity

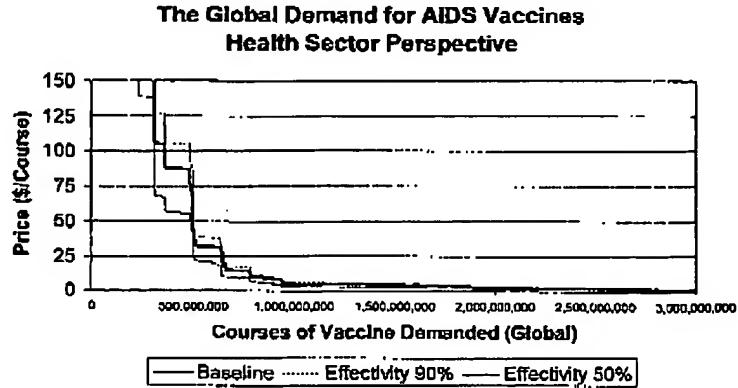


Fig. 1. Number of potential vaccine buyers as a function of the price of a complete course of vaccine. Solid line defines potential buyers using the health sector model (Eq. (1)) and assumes full course of vaccine lowers each recipient's AIDS risk by 75% for exactly 10 years. Dotted lines assume different rates of vaccine effectiveness.

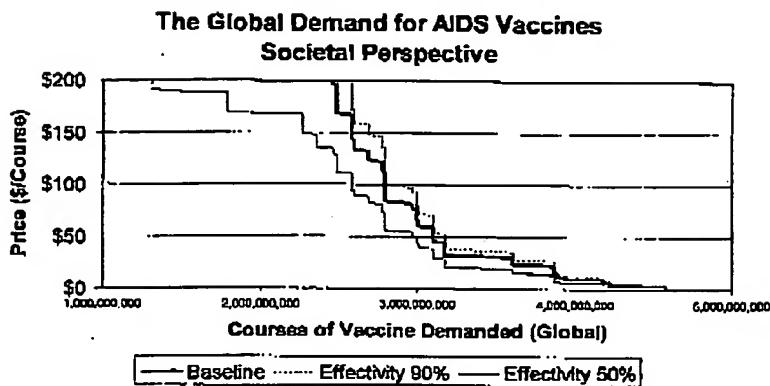


Fig. 2. Number of potential vaccine buyers as a function of the price of a complete course of vaccine. Solid line defines potential buyers using the societal model (Eq. (2)) and assumes full course of vaccine lowers each recipient's AIDS risk by 75% for exactly 10 years. Dotted lines assume different rates of vaccine effectiveness.

to the cost assumptions and incidence assumptions generate similar plots to those in Figs. 1 and 2, and are available elsewhere [10].

4. Discussion

One limitation of the model is the quality of the data on which it is based. Estimates of HIV seroincidence for many important subpopulations are not precisely known. Aggregating incidence rates across large geographic regions can obscure the dissimilarities between many individual countries and their regional geographic neighbors. Regional aggregates were used for all countries except east Asia where seroincidence and economic consequences of HIV/AIDS were so dissimilar between Japan, China, and South Korea that these three countries had to be analyzed separately from the rest of east Asia.

Another limitation is the application of population derived disease risk measures to individuals. Risk is a population measure and for a disease like HIV/AIDS many people are able to take steps to control that risk through individual behavioral change. The population incidence rates observed in

necessarily increase the cost of 1 year of treatment for established AIDS patients in developed countries [11].

The essential result of Table 1 is that the economic benefits of prevented medical spending per patient vaccinated are highest in developed countries and lowest in less developed countries. *This is opposite to where the greatest epidemiological benefit would be.* Although the financial benefits from AIDS vaccines are lower in developing countries, our models suggest that it is premature to write off regions like Latin America, the Caribbean, south and SE Asia as regions where the market cannot assist in the distribution of vaccines. Our model shows that health ministries in many less developed regions of the world are likely to find it cost-beneficial to actively purchase AIDS vaccines for selected populations at non-negligible prices. The societal perspective (Table 3 and Fig. 2) can be interpreted to indicate that given the opportunity to make their own purchase, a significantly large proportion of the developing world would find it cost-beneficial to buy an AIDS vaccine.

Although investments in technology can often make products better and cheaper later in the product lifecycle, one must contemplate the genuine possibility of several years spent with an AIDS vaccine whose production costs are high